Movement Disorders
CLINICAL PRACTICE

EDITORIAL COMMENTARY

# Once STN DBS, Always STN DBS?—Clinical, Ethical, and Financial Reflections on Deep Brain Stimulation for Parkinson's Disease

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At the 11th Parkinson's Disease symposium in Rome in March 1994, where neurologist Pierre Pollak presented, for the first time, the results of DBS of the STN, the late Professor David Marsden publicly stated that this was the most important discovery since levodopa.[1] This statement remains true today for selected patients with Parkinson's disease (PD) whose disease is still dopa responsive, but who suffer from disabling fluctuations and dyskinesias.

In this issue, a report by Rajan et al. from Kerala, India,[2] decribes 2 patients who had successful STN DBS for several years, in whom a fulminant parkinsonian crisis occurred when the battery was depleted, and the patients could not afford to pay for an emergency replacement of the neurostimulator.

The two 51- and 54-year-old patients had had PD for 11 years when they received STN DBS, and surgery was so successful that they could decrease their dopaminergic drug intake by 80% and 60%, respectively. Both patients developed an abrupt severe parkinsonian state, including severe rigidity, akinesia, and dysphagia, when the battery was depleted, 7 years post-DBS in 1 patient and 5 years post-DBS in the other (who already had one stimulator change 6 years after the primary DBS operation). One patient developed also malignant hyperthermia and the other suffered aspiration pneumonia and respiratory failure. Both patients received intensive care as well as high doses of enteral liquid L-dopa, pramipexole, and amantadine without any improvement in their condition. Financial issues could eventually be arranged so that 1 patient could have the stimulator replaced 11 days later, and the other patient 8 days later, and in both patients there was dramatic improvement when the stimulation was reinstated. As the researchers point out, and judging from the sparse literature about these certainly under-reported events, their patients were lucky to have survived this long-lasting, potentially fatal STN DBS withdrawal period, which, in this case, was solely the result of lack of immediate financial means for the patients to pay for the new stimulators. This report is indeed very important in that it raises several issues related to PD and STN DBS, issues that unfortunately are seldom discussed in the public domain.

## From Chronic Slowly Progressive Disease to Acute Life-Threatening Disease

In a "Clinical/Scientific Note" published in the *Movement* Disorders journal in January 2001, Hariz and Johansson were the first to draw attention to the consequences of an abrupt cessation of chronic STN DBS in PD patients, describing how this therapy can indeed be disease changing in as much as it transforms a typically slowly progressive disease into an acute condition with severe "rebound" of PD symptoms requiring emergency care, if chronic STN stimulation suddenly fails.[3] These researchers did report at that time that even an increase of dopaminergic medications, including fast-acting L-dopa, did not help the patients' acute deterioration, and it was first the reinstatement of the STN-DBS therapy that was able to reverse the worsening condition.[3]

## Lack of Response to Dopaminergic Drugs and Yet a Good Response to STN DBS

It is intriguing that the administration of high doses of dopaminergic drugs in patients with sudden withdrawal of STN DBS does

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not reverse the sudden parkinsonian crisis. This issue is discussed in the present report from Kerala, as well as in the few similar reports in the literature.[4,5] Reuter et al., from Kiel, Germany, recently reported on 3 patients in whom cessation of stimulation resulting from removal of infected hardware resulted in malignant parkinsonian state leading to death in 2 of the 3 patients.[4] These patients had suffered from PD for more than 18 years and had had DBS for more than 8 years. The patients had had previously three planned uneventful neurostimulator changes, with a 4- to 6-year interval since their first DBS operation, and suffered infection of hardware and its removal after the last operation. They were then treated with high doses of duodopa, apomorphine and amantadine to no avail, and their best motor UPDRS scores on medication still reached 90 points! In the patient who survived, a new neurostimulator could be implanted 2 months later and resulted in a dramatic improvement. The researchers speculated about the reasons why dopaminergic medications were no longer effective, but STN DBS still was, in the patient who survived until he could be reoperated. They concluded that STN-DBS withdrawal can be life threatening, "because the whole range of dopaminergic and nondopaminergic medical treatments may be ineffective at this stage."

The patients from Kerala also received all available medications during their DBS withdrawal state, except that the expensive duodopa and apomorphine were, for obvious financial reasons, not available to them. It is interesting to note that the most potent dopamine agonist, apomorphine, which used to be one of the cheapest ex-tempore medications since it was introduced in treatment of PD by neurologists Robert Schwab, Gerald Stern, and Andrew Lees, is no longer available except in its expensive patented preparations as Apopen or Apo pump.

Some issues that may predispose for STN-DBS withdrawal syndrome, and that were common both in the patients from Kerala and in those from Kiel, were an early age of onset of PD, a long duration of disease, an advanced state of disease at surgery, and an efficient STN DBS leading to a radical decrease of dopaminergic medication.

In any case, it remains puzzling why high doses of dopaminergic drugs were of no help to the patients upon cessation of chronic STN stimulation. Could the refractoriness to dopaminergic medication be owing to postsynaptic changes in striatal dopamine receptor affinity in the striatal neurons and striatal dendritic degeneration with a loss of dopaminergic synapses?

## Longevity of DBS Batteries, Financial Implications for Patients and Informed Consent

Notwithstanding the real risk for infections—that can occur anytime after the hardware is implanted, and that are in fact more common upon repeated surgery for replacement of stimulators with depleted batteries[6]—the fact that DBS is a lifelong therapy, and the issue of longevity of batteries, are highly relevant issues in countries where DBS is not reimbursed. For a few years, rechargeable neurostimulators have been available, but they are even more expensive and are not suitable for many patients with PD. Furthermore, the new, now commonly used, brands of nonrechargeable stimulators from the leading manufacturer seem to have batteries that last less than the previous most commonly used ones. Indeed, the patients from Kerala had had a Kinetra neurostimulator (Kinetra; Medtronic, Inc., Minneapolis, MN) that had a reasonable battery longevity (6–7 years, or more). For a few years, this model has not been available anymore, which will result in more frequent stimulator replacements in the future for patients who cannot have a rechargeable device. The financial implications for patients are obvious, and it is mandatory to inform patients of this before the first DBS surgery. It is equally important to inform patients that, in most cases, the so-called "reversibility" of DBS does not apply after a few years of STN DBS, and that cessation of this therapy does not mean that patients can just return to their oral medication as if nothing happened, and that the sudden worsening of PD that can occur after withdrawal of STN DBS cannot be simply attributed to a "progression of disease." The informed consent of a patient to STN DBS should be based not only on information about the risks of deep brain surgery, including hemorrhage, infection, and so on, but also about the likelihood that patients will be dependent for the rest of their life on this therapy, and that, in most cases, "once STN DBS, always STN DBS."

The issue of using the globus pallidus internus (GPi) as an alternative and more lenient target for primary DBS is discussed by Rajan et al., and the researchers rightly point out that cessation of this therapy, for any reason, may not lead to parkinsonian crisis given that patients usually remain on medication during chronic GPi DBS.

Another issue of relevance, especially in developing countries, is the role of stereotactic lesions, such as pallidotomy,[7,8] and subthalamic nucleotomy.[9] Pallidotomy for PD is officially considered by the International Parkinson and Movement Disorder Society as evidence based and efficient in advanced PD.[10] Yet it seems that it is no longer included in the surgical armamentarium of functional neurosurgeons. Aside from being a nonexpensive procedure,[8] it may be quite effective in breaking the vicious circle of a sudden parkinsonian crisis and also of a dystonic crisis, stemming from abrupt cessation of chronic DBS, or from any other reason.[11–13]

In summary, the report of Rajan et al. is highly relevant and needs to be reflected upon by clinicians suggesting STN DBS to patients, and by those who deal with patients on chronic STN DBS, especially—but not solely—in countries where this surgery is not covered by national health services.

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